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4-(1-Adamantylamino)-2-amino-6-methoxy-5-nitrosopyrimidine

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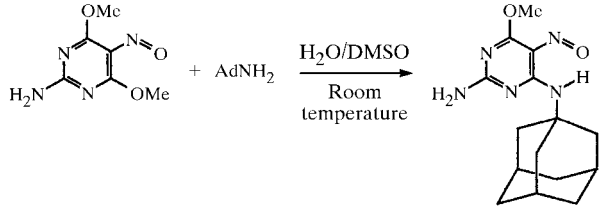
The title compound, $C_{15}H_{21}N_5O_2$, lies on a crystallographic mirror plane and is hydrogen bonded to neighbouring molecules by infinite chains formed by combinations of strong N—H···N and soft C—H···O hydrogen bonds. The pyrimidine moiety shows extensive delocalization.

Comment

Compounds containing the adamantanyl subunit have long been of interest to chemists due to its rigid structure and well defined substitution chemistry (Bingham & von Schleyer, 1971). Furthermore, the discovery of the potent antiviral activity of amantadine (1-adamantanamine) and rimantidine (*N*-methyl-1-adamantylmethylamine) has stimulated interest in the synthesis of adamantane-containing compounds (Kirschbaum, 1983). Many articles highlight investigations of molecules in which various biological activities are enhanced by the presence of an adamantyl block (Hedayatullah *et al.*, 1999). This is specifically due to the strong lipophilic character of the adamantyl group and the high resistance to metabolic degradation of the compounds containing this group (Sasaki *et al.*, 1979; Galpin *et al.*, 1979).

The title compound, (II) (Fig. 1), was prepared during the course of our investigations into the activation to nucleophilic substitution which a 5-nitroso group produces on methoxy groups linked to positions 2- and 4(6)- of a pyrimidine system. The 1-adamantyl moiety is a very bulky group whose steric requirements seriously hinder the participation of 1-adamantylamine as a nucleophile in substitution reactions. The resolution of the structure of (II) by X-ray diffraction analysis unambiguously confirms that this compound forms by aminolysis of (I), instead of the adamantylammonium salt that could be produced by base-catalysed hydrolysis of (I). The latter is a process which competes with aminolysis in aqueous media when strong steric hindrance exists, as was proven by the synthesis of piperidinium 6-amino-3-methyl-5-nitroso-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-ide (Low *et al.*, 1999). The formation of (II) proves that methoxy groups in nitroso derivatives are so activated towards nucleophilic substitution that even bulky amines such as adamantylamine are capable of effecting nucleophilic substitution at room temperature.



(I) (II)

The molecular dimensions of (II) show a similar delocalization to that found in the *N*-(6-amino-3,4-dihydro-3-methyl-5-nitroso-4-oxopyrimidin-2-yl) derivatives of glycine, valine, serine, threonine and methionine described by Low *et al.* (2000). The only significant difference in the bond lengths is the presence of the N3═C4 double bond in (II).

A feature of interest in the structure is the fact that the molecule lies on a crystallographic mirror plane at $(0,\frac{1}{4},0)$. This passes through the plane of the pyrimidine moiety and its substituents and two of the C atoms of the adamantanyl moiety. This is a consequence of the fact that the adamantanyl moiety is a substituent on N6, an amino group, which has a marked degree of sp^2 character, as evidenced by the C6—N6 bond length of 1.336 (5) Å. This is a common feature of 6-aminopyrimidines.

A strong N—H···N intermolecular hydrogen bond between N2 and N5^{i} [symmetry code: (i) $x, y, 1 + z$] links the molecules into a $C(6)$ motif which forms, by translation, an infinite chain along [001]. Furthermore, an intramolecular hydrogen bond between N6 and O5 helps to stabilize this planarity. A soft intermolecular C—H···O bond between C67 and O5^{i} has the effect of pulling two of the adamantane C atoms into the plane of the pyrimidine moiety. These soft hydrogen bonds form a $C(7)$ motif, generating an infinite chain along [001] by translation. The $C(6)$ and $C(7)$ motifs combine to produce an $R_2^2(13)$ ring structure (Fig. 2), which lies with the chain structures on the crystallographic mirror plane. The

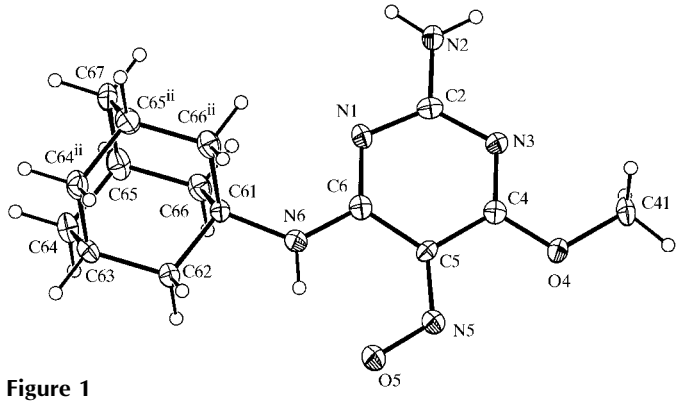


Figure 1
A view of (II) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The H atoms on the methyl C41 atom are disordered and for clarity only one set is shown. [Symmetry code: (ii) $x, \frac{1}{2} - y, z$.]

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second amino-H atom attached to N2 is not involved in hydrogen bonding, this being prevented by the steric bulk of the adamantane. Examination of the structure with *PLATON* (Spek, 2000) showed that there were no solvent-accessible voids in the crystal lattice.

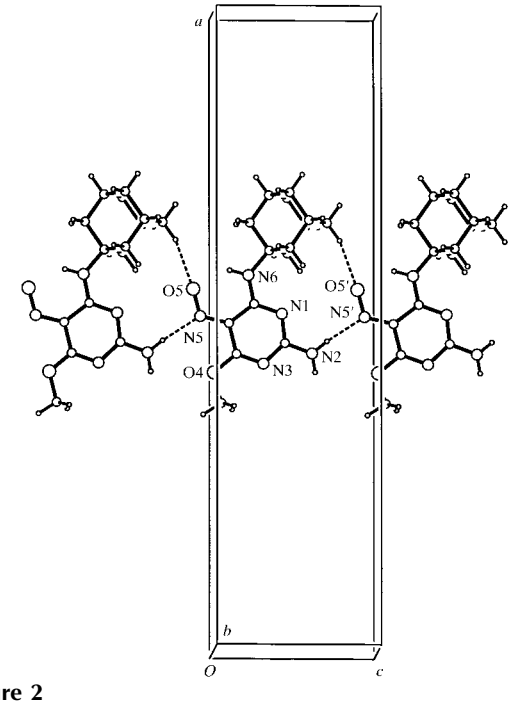

Figure 2
A view of the crystal structure of (II) showing the hydrogen-bonding motifs formed by unit translations along [001] [symmetry code: (′) x, y, $1 + z$].

Experimental

1-Adamantanamine (0.46 g, 3 mmol, 1.5 equivalents) was added to a solution of (I) (0.368 g, 2.00 mmol) in DMSO/H_2O (3:2 *v*/*v*, 25 ml). The mixture was stirred at room temperature and monitored by thin-layer chromatography (eluent CH_2Cl_2/MeOH, 9:1 *v*/*v*) until a pink suspension was obtained after 36 h. The precipitate was filtered, washed with water and acetone, dried over blue silica and recrystallized from methanol/acetone to give crystals of (II) (yield 0.53 g, 87%; decomposition > 473 K). Analysis calculated for $C_{15}H_{21}N_5O_2$: C 59.36, H 6.98, N 23.09%; found: C 59.34, H 7.01, N 22.85%. Full IR, ^{1}H and ^{13}C NMR, and MS spectral data have been deposited.

Crystal data

$C_{15}H_{21}N_5O_2$
M_r = 303.37
Orthorhombic, *Pnma*
a = 29.207 (2) Å
b = 6.5860 (4) Å
c = 7.4782 (4) Å
V = 1438.48 (16) Å^3
Z = 4
D_x = 1.401 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1463 reflections
θ = 1.39–25.93°
μ = 0.097 mm^{-1}
T = 150 (1) K
Block, pink
0.15 × 0.15 × 0.10 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
T_{min} = 0.986, T_{max} = 0.990
8692 measured reflections
1463 independent reflections
712 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
θ_{max} = 25.93°
$h = -35 \rightarrow 0$
$k = 0 \rightarrow 8$
$l = -9 \rightarrow 0$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.060
$wR(F^2)$ = 0.181
S = 0.91
1463 reflections
124 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.106P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.37 e Å^{-3}
$\Delta\rho_{min}$ = −0.40 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.351 (5)	N3—C4	1.297 (5)
N1—C6	1.336 (5)	N5—O5	1.286 (4)
N2—C2	1.321 (5)	N5—C5	1.338 (5)
N3—C2	1.364 (5)	N6—C6	1.339 (5)
O5—N5—C5	117.9 (3)	C6—N6—C61	129.1 (4)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N6—H6···O5	0.88	1.87	2.589 (5)	138
N2—H2A···N5^{i}	0.88	2.05	2.928 (5)	174
C67—H67A···O5^{i}	0.99	2.38	3.342 (5)	164

Symmetry code: (i) x, y, $1 + z$.

The C41 methyl H atoms were disordered and were allowed for by placing six H atoms with suitable occupancies around C41. H atoms were treated as riding, with C—H = 0.98–1.00 Å and N—H = 0.88 Å.

Data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *DENZO*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2000); software used to prepare material for publication: *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC X-ray Crystallographic Service, University of Southampton. The authors thank the staff for all their help and advice.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1029). Services for accessing these data are described at the back of the journal.

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